

IN THE CLAIMS:

Please cancel Claim 2.

Please substitute the following claims for the previously pending claims. A copy of the claims showing marked changes is provided in an attachment hereto. A copy of all pending claims, as amended, is also provided in an attachment hereto for the Examiner's convenience.

B 1 mb 1 71. (Amended) A multivalent vaccine composition comprising at least two recombinant variable regions of immunoglobulin molecules derived from B-cell lymphoma cells, wherein said at least two variable regions comprise recombinant immunoglobulin molecules that differ by at least one idiotope.

3. (Amended) The vaccine composition of Claim 1, wherein said recombinant immunoglobulin molecules are covalently linked to an immune-enhancing cytokine.

mb 417 4. (Amended) The vaccine composition of Claim 3, wherein said cytokine is selected from the group consisting of granulocyte-macrophage colony stimulating factor, interleukin-2 and interleukin-4.

B 2 5. (Amended) The multivalent vaccine composition of Claim 1 further comprising at least one pharmaceutically acceptable excipient.

6. (Amended) The multivalent vaccine composition of Claim 1 further comprising an adjuvant.

(Please add the following claims:)

25. (New) A vaccine composition produced according to a method comprising:

a) providing:

i) malignant B cells isolated from a patient having a B-cell lymphoma;

- ii) an expression vector;
- iii) an amplification vector comprising a recombinant oligonucleotide having a sequence encoding a first inhibitable enzyme operably linked to a heterologous promoter; and
- iv) a T lymphoid parent cell line;
- b) isolating nucleic acid from said malignant cells, said nucleic acid comprising nucleotide sequences encoding at least one V_H region and at least one V_L region, said V_H and V_L regions derived from immunoglobulin molecules expressed by said malignant cells;
- c) inserting said nucleotide sequences encoding said V_H and V_L regions into said expression vector;
- d) introducing said expression vector and said amplification vector into said parent cell line to generate one or more transformed cells;
- e) growing said transformed cells in a first aqueous solution containing an inhibitor capable of inhibiting said first inhibitable enzyme wherein the concentration of said inhibitor present in said first aqueous solution is sufficient to prevent growth of said parent cell line; and
- f) identifying a transformed cell capable of growth in said first aqueous solution, wherein said transformed cell capable of growth expresses said V_H and V_L regions wherein V_H and V_L regions comprise a protein molecule useful as said vaccine.
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26. (New) The composition of Claim 25, wherein nucleotide sequences encoding said V_H and V_L regions comprise at least two V_H and at least one V_L regions.

27. (New) The composition of Claim 25, wherein nucleotide sequences encoding said V_H and V_L regions comprise at least one V_H and at least two V_L regions.

28. (New) A vaccine composition produced according to a method comprising:

a) providing:

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- i) malignant B cells isolated from a patient having a B-cell lymphoma;
 - ii) an expression vector;
 - iii) an amplification vector comprising a first recombinant oligonucleotide having a sequence encoding a first inhibitable enzyme operably linked to a heterologous promoter;
 - iv) a selection vector comprising a second recombinant oligonucleotide having a sequence which encodes a selectable gene product; and
 - v) a T lymphoid parent cell line;
- b) isolating nucleic acid from said malignant cells, said nucleic acid comprising nucleotide sequences encoding at least one V_H region and at least one V_L region, said V_H and V_L regions derived from immunoglobulin molecules expressed by said malignant cells;
- c) inserting said nucleotide sequences encoding said V_H and V_L regions into said expression vector;
- d) introducing said expression vector, said amplification vector and said selection vector into said parent cell line to generate transformed cells;
- e) introducing said transformed cells into a first aqueous solution, said first aqueous solution requiring the expression of said selectable gene product for growth of said transformed cells;
- f) identifying at least one transformed cell capable of growth in said first aqueous solution;
- g) introducing said transformed cell capable of growth in said first aqueous medium into a second aqueous solution, said second aqueous solution comprising an inhibitor capable of inhibiting said first inhibitable enzyme, wherein the concentration of said inhibitor present in said second aqueous solution is sufficient to prevent growth of said parent cell line; and
- h) identifying at least one transformed cell capable of growth in said second aqueous solution, wherein said transformed cell capable of growth

expresses said V_H and V_L regions wherein said V_H and V_L regions comprise a protein molecule.

29. (New) A vaccine composition produced according to a method comprising:

a) providing

- i) malignant B cells isolated from a patient having a B-cell lymphoma;
- ii) an expression vector;
- iii) an amplification vector comprising a first recombinant oligonucleotide having a sequence encoding a first inhibitable enzyme operably linked to a heterologous promoter;
- iv) a selection vector comprising a second recombinant oligonucleotide having a sequence which encodes a selectable gene product; and
- v) a T lymphoid parent cell line;

b) isolating nucleic acid from said malignant cells, said nucleic acid comprising nucleotide sequences encoding at least one V_H region and at least one V_L region, said V_H and V_L regions derived from immunoglobulin molecules expressed by said malignant cells;

c) inserting said nucleotide sequences encoding said V_H and V_L regions into said expression vector;

d) introducing said expression vector, said amplification vector and said selection vector into said parent cell line to generate transformed cells;

e) introducing said transformed cells into a first aqueous solution, said first aqueous solution requiring the expression of said selectable gene product for growth of said transformed cells;

f) identifying at least one individual clone of transformed cells capable of growth in said first aqueous solution;

g) introducing said individual clone capable of growth in said first aqueous solution into a second aqueous solution, said second aqueous solution comprising an inhibitor capable of inhibiting said first inhibitable enzyme, wherein the concentration

of said inhibitor present in said first aqueous solution is sufficient to prevent growth of said parent cell line; and

h) identifying at least one individual clone capable of growth in said second aqueous solution, wherein said clone capable of growth expresses said V_H and V_L regions wherein said V_H and V_L regions comprise a protein molecule.

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30. (New) A multivalent vaccine composition comprising at least two recombinant variable regions of immunoglobulin molecules derived from B-cell lymphoma cells, wherein said cells express at least two different immunoglobulin molecules, said immunoglobulin molecules differing by at least one idiotope, wherein said at least two recombinant variable regions of immunoglobulin molecules are derived by a method comprising the step of amplifying cDNA for said variable regions from mRNA from said B-cell lymphoma cells using amplification primers complementary to conserved sequences flanking said variable regions.

31. (New) The vaccine composition of Claim 1, wherein said recombinant immunoglobulin molecules are conjugated to a foreign carrier protein.

32. (New) The vaccine composition of Claim 31, wherein said foreign carrier protein comprises keyhole limpet hemocyanin.

REMARKS

Claims 1-24 were originally filed in a parent case. Claims 1-6 were elected for prosecution in this divisional application. Claims 25-32 are added with this amendment. In the Office Action dated December 19, 2000, the Examiner made a number of arguments and rejections. For clarity, the rejections at issue are set forth by number in the order they are herein addressed:

- (1) Claims 1-6 stand rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite; and
- (2) Claims 1-6 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable in view of Tao and Levy (Nature 362:755 [1993]; hereinafter